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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/373,230	08/12/1999	HARUKI OKMURA	OKAMURA=2E	2359

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EXAMINER
JIANG, DONG

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 03/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/373,230	OKMURA ET AL.	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 December 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,11,14 and 15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *7-9* is/are allowed.

6)☒ Claim(s) *1-6 and 11, 14 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. *08/505,535* .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED OFFICE ACTION

The request filed on 23 January 2002 (paper No. 11) for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/373,230 is acceptable and a CPA has been established. An action on the CPA follows.

Applicant's amendment in paper No. 8 filed on 19 December 2001 is acknowledged and entered. Following the amendment, claims 1-3, 7, 8, 11 and 14 are amended, and claims 12 and 13 are canceled.

Currently, claims 1-9, 11, 14 and 15 are pending and under consideration.

Withdrawal of Objections and Rejections:

The objections of the specification are withdrawn in view of applicant's amendment and argument.

All objections and rejections of claims 12 and 13 are moot as the applicant has canceled the claim.

The new matter rejection of claims 1-3, 7 and 11 under 35 U.S.C. 112, first paragraph is withdrawn in view of applicant's amendment.

The rejection of claims 1, 2, 7-9, 14 and 15 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn in view of applicant's amendments.

Objections and Rejections under 35 U.S.C. §112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-6 and 11 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons set forth in the last Office Action, paper No. 7, mailed on 03 July 2001, at page 4.

Applicants argument, filed on 19 December 2001 (paper No. 8) has been fully considered, but is not deemed persuasive for reasons below.

At page 11 of the response, the applicant argues that "not substantially altering" means "substantially the same", that this language is not indefinite as the Court of Appeals suggested in *Arnold Pipe Rentals Company, Inc. v Engineering Enterprises*, 146 USPQ 416, that "at least substantially flat" is not fatally indefinite, and that two US patents accepted the use of the claim language "substantially the same". This argument is not persuasive because it is noted that the term "substantially" in the examples presented by the applicants is used to describe the degree of a physical feature ("substantially flat"), or the level of an activity (US 5,429,936, claim 11), or used in a method claim, rather than a product claim (US 6,156,315, claim 2). On the other hand, the term "substantially" in the instant claim is used to describe an amino acid sequence (part (4) of the claim). A skilled artisan would not be able to envision the detailed sequence structure of the encompassed proteins which have "substantially the same" sequence as that described in the claim limitation. The metes and bounds of the claim, therefore, cannot be unambiguously determined. Additionally, each patent application is examined and prosecuted on its own merit, and the Examiner cannot comment on the prosecution of the other patent.

The remaining claims are rejected for depending from an indefinite claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-6 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited in scope to a specific variant of said protein, which has an amino acid sequence of SEQ ID:2 where residue 70 is methionine or threonine, does not reasonably provide enablement for with claims to variants having physicochemical and functional properties listed in parts (1) to (4) of claim 3, and having the amino acid sequence of SEQ ID NO:2 with at least one amino acid residue in SEQ ID:2 replaced with different amino acid, or at least one amino acid residue deleted or added to the

N-terminus of SEQ ID:2 while not substantially altering physicochemical properties of the protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims, for the reasons set forth in the last Office Action, paper No. 7, at pages 3-4.

Applicants argument in paper No. 8 has been fully considered, but is not deemed persuasive for reasons below.

At pages 13 and 14 of the response, the applicant argues that at the time claimed invention was made, it was possible for the skilled artisan to obtain the claimed variants based on the sequence of SEQ ID NO:2, and to screen for variants based on the properties in claim 3 without undue experimentation. This argument is not persuasive because the main issue is not whether a skilled artisan is able to generate and test the variants of SEQ ID NO:2 with the claimed physicochemical properties, rather, the issue is that the claim limitation in Part (4) of claim 3 that "wherein said variant has the amino acid sequence of SEQ ID NO:2 with at least one amino acid residue in SEQ ID NO:2 replaced ..." reads on a functional equivalent of IGIF with the cited physicochemical properties, which *may not be a sequence variant of SEQ ID NO:2* as there is no upper limit in the claim as to how many amino acid residues may be replaced. And such a functional equivalent is not described in the specification, thus, the specification fails to teach how to make a commensurate number of such species, and undue experimentation would be required of the skilled artisan to make the claimed invention in its full scope.

Claims 1, 2, 11, 14 and 15 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited in scope to a protein with SEQ ID NO:2, wherein residue 70 is methionine or threonine, does not reasonably provide enablement for variants with properties listed in these claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims, for the reasons set forth in the last Office Action, paper No. 7, at pages 5-7.

Applicants argument in paper No. 8 has been fully considered, but is not deemed persuasive for reasons below.

At page 15 of the response, with respect to claim 11, the applicant argues that the variants in the amended claim 11 are obtainable without undue experimentation based on the sequence of SEQ ID NO:2 and the state of the art. This argument is not persuasive because, once again, the issue is not whether a skilled artisan is able to generate and test the variants of SEQ ID NO:2 with the claimed physicochemical properties, rather, the issue is that the claim limitation merely requires a *variant* having one antigenic fragment of SEQ ID NO:2, and reacting with a mAb specific to SEQ ID NO:2, or a *variant* having the amino acid sequence of SEQ ID NO:2 with at least one amino acid residue in SEQ ID NO:2 replaced ..." reads on a functional equivalent of IGIF with the cited physicochemical properties, which *may not be a sequence variant of SEQ ID NO:2* as the only sequence limitation is one antigenic fragment of SEQ ID NO:2, which can be 4 amino acids, or there is no upper limit as to how many amino acid residues may be replaced. And such a functional equivalent is not described in the specification, thus, the specification fails to teach how to make a commensurate number of such species, and undue experimentation would be required of the skilled artisan to make the claimed invention in its full scope.

Claims 1-6, 11, 14 and 15 remain further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons set forth in the last Office Action, paper No. 7, at pages 7-8.

Applicants argument in paper No. 8 has been fully considered, but is not deemed persuasive for reasons below.

At page 14 of the response, the applicant argues that the Examiner's requirement is not a realistic one, and it is impossible to check if a monoclonal antibody to a certain polypeptide binds to other polypeptides and disclose the results in the specification. This argument is not persuasive because the Examiner has not required such. The issue is that *the functional variants* which mrerly share a few amino acids with SEQ ID NO:2, and react with a monoclonal antibody not specifically reacting with SEQ ID NO:2 are *not described* in the specification, and therefore, it does not reasonably convey to one skilled in the relavant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5, 6, 11, 14 and 15 remain rejected under 35 U.S.C. 102(b) as being anticipated by Nakamura *et al.* (*Infect. Immun.* 61: 64-70, 1993), for the reasons set forth in the previous Office Actions, paper No. 4, at page 7, and paper No. 7, at pages 9-10.

Applicants argument in paper No. 8 has been fully considered, but is not deemed persuasive for reasons below.

With respect to claims 3, 5 and 6, the applicant argues, at pages 15 to 17 of the response, that the protein factor of Nakamura is distinct from the presently claimed protein as the present protein shows a molecular weight of 19 kDa on SDS-PAGE, whereas the factor of Nakamura is 50-55 kDa, that there are no descriptions in Nakamura suggesting the factor is a polymer of the IGIF of the claimed invention, and that Nakamura's factor loses the activity when treated on SDS-PAGE. This argument is not persuasive because applicants completely ignored the evidence in the references provided by the Examiner, which are the subsequent studies of Nakamura's factor by the same group, and indicate that the prior art protein is the same as that of the present invention. The teachings and relevance of the supporting references cited are reiterated herein. Okamura et al. (Infection and Immunity, 1995, 63(10):3966-72) discloses a purified murine IGIF from the liver with the same physiochemical and biological properties as the claimed IGIF, and further indicates that the same molecule was also demonstrated in the serum factor that was previously reported (by Nakamura) to have an apparent molecular mass of 75 kDa by gel filtration (and 50-55 kDa on SDS-PAGE). Moreover, Okamura demonstrates that the molecular mass of 75 kDa IGIF was reduced to 19 kDa on 0.1% SDS-PAGE in the presence of DTT, and the N-terminal amino acid sequence is the same as that of IGIF from the liver, "thus IGIF in the serum sample was proved to be the same IGIF as that found in the liver exact "(the abstract, and page 3969, the second paragraph of the left column). Therefore, the protein factor

of Nakamura anticipates the invention in claims 3, and 5-6. Additionally, a later publication from the same laboratory (Ushio *et al., J. Immunol.* 156: 4274-4279, 1996, provided by the applicants) evidences that the 18-19 kDa murine factor described by in the Okamura paper has an amino acid sequence (Fig. 2) which is identical to that shown in instant SEQ ID NO: 2. In view of the similar sources and the identity of structural, biophysical, and functional properties of the instantly claimed protein and the 18-19 kDa factor described in the Okamura and Ushio papers, it reasonably appears that they are the same.

With respect to the alleged difference in the activity between Nakamura's factor and that of the present invention after treated on SDS-PAGE, the Examiner notices that at page 23 of the specification, Example 2-1, it merely states that the purified protein was electrophoresed in a SDS-PAGE to mainly show a single protein band with an IFN-γ inducing activity, which does not indicate that the protein after SDS-PAGE has the activity. As shown in the functional assays in Example 2-4, "a present purified protein" is used in the assays. In view of Example 1, which is directed to "preparation of purified protein", "a present purified protein" used in the functional assays demonstrated in Example 2-4 is purified using the procedure in Example 1, not from SDS-PAGE. Therefore, the "difference" between Nakamura's factor and the protein of the present invention in IFN-γ inducing activity of the protein after treatment on SDS-PAGE is not credible, and cannot be used to support the assertion that the two proteins are distinct.

Conclusion:

Claims 7-9 are allowable.

Advisory Information:

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 703-305-1345. The examiner can normally be reached on Monday - Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER

Dong Jiang, Ph.D.
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AU1646
3/18/03